JACC: CASE REPORTS VOL. 18, 2023

CASE REPORT

BEGINNER

CLINICAL CASE

Rare Variant of Meigs Syndrome Associated With Pericardial Effusion

Michael Gianarakis, MD,[a] Beni Verma, MD,[b] Nikita Verma,[c] Cyrus Marwaha,[d] Robert Pollard, MD,[e] Meera Kondapaneni, MD,[b] Aisha Siraj, MD,[b] Najmul I. Siddiqi, MD[b]

ABSTRACT

Meigs syndrome is an uncommon entity associated with benign ovarian tumor, pleural effusion, and ascites. Its association with pericardial effusion is extremely rare. We report a case of Meigs syndrome associated with recurrent pericardial effusion that resolved after surgical resection of the ovarian tumor. (**Level of Difficulty: Beginner.**) (J Am Coll Cardiol Case Rep 2023;18:101927) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 56-year-old woman with paranoid schizophrenia was evaluated by gynecology for abdominal discomfort. On a computed tomography scan of the abdomen and pelvis, she was found to have a solid, right-sided adnexal mass measuring 7.3 × 6.2 × 4.5 cm, with small amount of ascites and moderate pericardial effusion (PEFF) (**Figure 1**). Subsequent workup with magnetic resonance imaging suggested that the mass may be mesenchymal or stromal in origin. CA-125 level was 5.9 U/mL (reference value, <35 U/mL), CA 19-9 was 24 U/mL (reference value, <35.1 U/mL), and carcinoembryonic antigen level was 2 ng/mL (reference value, <3.0 ng/mL). She was referred for surgical opinion to consider resection of the adnexal mass; however, she required inpatient treatment for acute episodes of schizophrenia. Seven months later, she reported gradual onset of dyspnea and was referred to cardiology. A transthoracic echocardiogram (TTE) was ordered, which exhibited a large PEFF with tamponade physiology (**Figure 2**). She was advised inpatient admission; however, she declined. Four days later, she presented to the emergency department with worsening symptoms and was admitted. Her blood pressure was 138/99 mm Hg, heart rate 76 beats/min, respiratory rate 18 breaths/min, and oxygen saturation 96% on room air. On physical examination, heart sounds were distant and

LEARNING OBJECTIVES

- To review Meigs syndrome, including possible pathogenesis, clinical presentation, and management.
- To discuss the diagnostic evaluation of patients with unexplained pericardial effusion.
- To recognize the importance of excluding ovarian mass in females with recurrent pericardial effusion.
- To explore the possible role of anti-inflammatory medications in patients with pericardial manifestations of Meigs Syndrome.

From the [a]Department of Internal Medicine, University of Illinois at Chicago, Chicago, Illinois, USA; [b]Department of Cardiology, Case Western Reserve University School of Medicine/MetroHealth, Cleveland, Ohio, USA; [c]Department of Internal Medicine, Baba Farid University of Health Sciences, Faridkot, Punjab, India; [d]Department of Biology, Penn State, Hershey, Pennsylvania, USA; and the [e]Department of Obstetrics/Gynecology, Case Western Reserve University/MetroHealth, Cleveland, Ohio, USA.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received February 14, 2023; revised manuscript received May 16, 2023, accepted May 25, 2023.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2023.101927

ABBREVIATIONS AND ACRONYMS

PEFF = pericardial effusion

TTE = transthoracic echocardiogram

the jugular venous pressure was elevated at 14 cm. No pulsus paradoxus, friction rub, gallop, or murmur were noted.

PAST MEDICAL HISTORY

Her past medical history was notable for type 2 diabetes mellitus, dyslipidemia, paranoid schizophrenia, and a remote, 3-pack-year smoking history. Family history was notable for ovarian cancer in her mother.

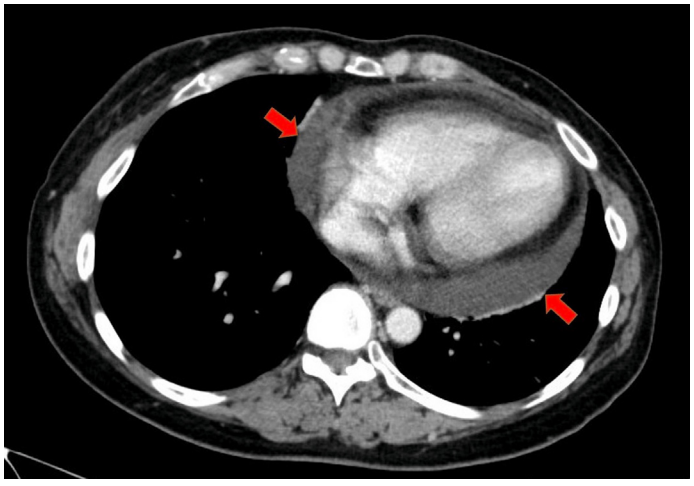
DIFFERENTIAL DIAGNOSIS

Given the radiographic characteristics of the pelvic mass and the patient's family history, malignant PEFF was strongly suspected. Other etiologies of PEFF considered were viral, autoimmune, or idiopathic.

INVESTIGATIONS

A chest radiograph revealed enlarged cardiac silhouette and small bilateral pleural effusions. An electrocardiogram showed normal sinus rhythm with low-voltage QRS. Initial laboratory workup, including troponin, was unremarkable. TTE showed 2.5-cm circumferential PEFF with tamponade physiology suggested by diastolic right ventricular collapse and exaggerated respiratory variation across mitral and tricuspid valves (Figure 2). Rheumatological investigations revealed positive antinuclear antibodies, low double strand DNA titer, and normal C3, C4, erythrocyte sedimentation rate, and C-reactive protein levels. Because the serum double strand DNA antibody by Crithidia IFA and antinuclear antibody by HEp-2 substrate were negative, there was very low suspicion for a connective tissue disorder.

FIGURE 1 Computed Tomography Scan of the Chest



Computed tomography of chest showing moderate circumferential pericardial effusion **(red arrows)**.

MANAGEMENT

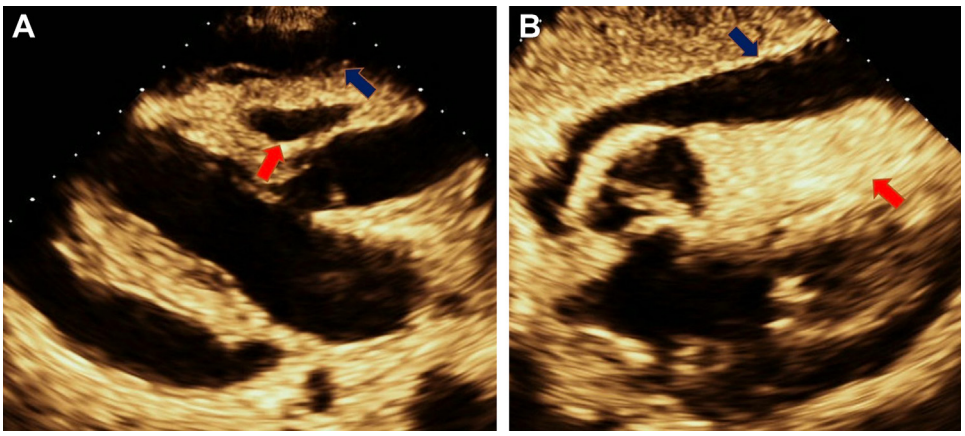
The patient underwent diagnostic and therapeutic pericardiocentesis to address symptomatic PEFF (shortness of breath on exertion with tamponade physiology suggested), yielding 600 mL of transudative serosanguineous fluid. The pericardial opening pressure was 9 mm Hg (reference value, ≤5 mm Hg). After this, she continued to drain 80 mL/day. Cytology revealed no evidence of malignant cells. Additionally, the fluid was negative for gram stain, adenosine deaminase and acid-fast bacilli; bacterial and fungal cultures showed no growth. Cardiac magnetic resonance demonstrated no evidence of pericardial inflammation (pericardial thickening or late gadolinium enhancement).

The pericardial drain was removed on day 5. TTE performed 48 hours later showed reaccumulation of PEFF graded as moderate (1.2 cm). Owing to the recurrence of PEFF, she was discharged on empiric anti-inflammatory therapy, colchicine 0.6 mg twice daily, and ibuprofen 600 mg 3 times daily. One week later, she was readmitted with fever secondary to urinary tract infection. Repeat TTE showed an interval increase of PEFF (1.9 cm), but without evidence of constriction or tamponade physiology. On account of recurrent PEFF in the setting of an ovarian mass, gynecology was consulted owing to suspicion of Meigs syndrome. Because her left ovary seemed to be fibromatous on imaging, on the recommendation of her gynecologist, she underwent laparoscopic bilateral salpingo-oophorectomy 2 months later. Her symptoms of shortness of breath on exertion resolved. Anti-inflammatory therapy was gradually tapered over 2 months. Histopathological examination of the resected masses was consistent with bilateral ovarian fibroma.

DISCUSSION

Meigs syndrome encompasses a rare clinical entity of benign ovarian tumor, most commonly ovarian fibromas, with pleural effusion and ascites. The syndrome occurs in 1% of ovarian tumors and is most common in postmenopausal women with an average age of onset at 50 years.[1] In 2005, the term, Meigs-like syndrome was used to describe the first reported case of Meigs syndrome with PEFF.[2] Three other cases of Meigs-like syndrome have been reported; however,

FIGURE 2 **Transthoracic Echocardiogram**



Parasternal long axis **(A)** and subcostal view **(B)** on transthoracic echocardiogram revealing a large pericardial effusion **(blue arrows)** with significant right ventricular collapse **(red arrows)**.

these cases had predominant pleural effusions with incidental PEFF, and ovarian fibroma was not histologically confirmed in those cases.[3-5] We report a histologically confirmed Meigs syndrome presenting with PEFF with tamponade physiology, recurrence of PEFF, and its resolution after resection. Our case is the first to present with bilateral fibromas, rather than unilateral. The cause-and-effect relationship was demonstrated by complete resolution of PEFF after resection of ovarian masses. Owing to a paucity of literature on this topic, our case report provides valuable information to further understand its clinical course. Accumulation of similar additional data in the future will help to refine management of this condition.

The mechanism of pleural and ascitic fluid collection in Meigs syndrome is unknown. The postulated hypotheses range from fluid leakage from edematous fibromas, dysfunction of abdominal and pelvic lymphatic system owing to physical pressure of the tumor, and migration of fluid through defects in the diaphragm.[6] Recent publications have suggested the role of inflammatory cytokines in increasing capillary permeability. Elevated serum, ascitic, and pleural fluid levels of inflammatory cytokines such as, vascular endothelial growth factor, fibroblast growth factor, and IL-6 have been found in patients with Meigs syndrome, with decreases in their levels after tumor resection.[7]

It is crucial to exclude malignancy while investigating PEFF. In a review of 173 consecutive patients who underwent pericardiocentesis, malignancy was the most common cause of effusion (33% cases).[8] Clinical features associated with malignant etiology include cardiac tamponade at presentation, recurrent pericarditis, and lack of response to nonsteroidal anti-inflammatory agents. In our case, the combination of PEFF and ovarian mass raised suspicion for a malignant effusion; however, the fluid was found to be transudative lacking neoplastic cells. Other causes of PEFF include connective tissue disease and infectious pericarditis were excluded based on serology and cardiac magnetic resonance results.

Surgical resection of the tumor is the definitive treatment for Meigs syndrome, leading to resolution of ascitic and pleural fluid within weeks.[6] Our patient also demonstrated resolution of PEFF after tumor resection. Given the likely role of inflammatory cytokines in the pathogenesis of Meigs syndrome, anti-inflammatory treatment may be beneficial. Owing to recurrence of PEFF, the patient was treated empirically with colchicine and ibuprofen. Subsequently, there was no recurrence of tamponade physiology, and symptoms were controlled until the tumor resection two months later. Given the clinical benefit seen in our patient, anti-inflammatory medications may have a role in patients with Meigs syndrome with pericardial manifestations, particularly in those with symptomatic PEFF awaiting surgical resection, recurrent PEFF refractory to pericardiocentesis, or in poor surgical candidates. Future observational studies are necessary to analyze the risk factors,

prevalence, and characteristics of pericardial disease in Meigs Syndrome and explore the role of anti-inflammatory agents.

FOLLOW-UP

TTE at 3 months after bilateral fibroma resection showed resolution of PEFF. Anti-inflammatory therapy was weaned off without recurrence of symptoms or PEFF. She continues to remain symptom free and attained her baseline functional capacity.

CONCLUSIONS

PEFF is a rare manifestation of Meigs syndrome and can present with cardiac tamponade. Our case represents this rare occurrence. This entity should be considered in the differential diagnosis of patients with ovarian masses and coexisting, unexplained recurrent or persistent PEFF. Owing to scant literature, its rare occurrence, and need for high clinical suspicion, this condition may remain undiagnosed. To date, surgical resection is the only effective treatment of Meigs syndrome. Anti-inflammatory medications may have a role in in the treatment of patients with Meigs syndrome with PEFF; however, further research is needed to investigate their efficacy.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Michael Gianarakis, 840 South Wood St (M/C 718), Room 440 Clinical Sciences North Building, Chicago, Illinois 60612, USA. E-mail: michaelgianarakis@gmail.com.

REFERENCES

1. Shiau C, Chang M, Hsieh C, Hsieh T, Chiang C. Meigs' syndrome in a young woman with a normal serum CA-125 level. *Chang Gung Med J*. 2005;28:587-591.

2. Qaisar S, Osman F, Pitt M. Resolution of pericardial effusion after removal of ovarian fibroma-a Meigs'-like syndrome. *J R Soc Med*. 2005;98:313-314.

3. Patanè S, Marte F, Di Bella G, Davi' M. Pericardial effusion with elevated serum carbohydrate antigen 125 levels and ovarian tumor mass. *Int J Cardiol*. 2008;127:105.

4. Arnáiz-García ME, González-Santos JM, López-Rodriguez J, Dalmau-Sorli MJ, Bueno-Codoñer ME, Arnáiz J. Meigs-like syndrome presenting as cardiac tamponade. *Rev Port Cardiol*. 2013;32:547-548.

5. Okuda K, Noguchi S, Narumoto O, Ikemura M, Yamauchi Y, Tanaka G, et al. A case of Meigs' syndrome with preceding pericardial effusion in advance of pleural effusion. *BMC Pulm Med*. 2016;10:16.

6. Meigs JV. Fibroma of the ovary with ascites and hydrothorax; Meigs' syndrome. *Am J Obstet Gynecol*. 1954;67:962-985.

7. Abramov Y, Anteby SO, Fasouliotis SJ, Barak V. Markedly elevated levels of vascular endothelial growth factor, fibroblast growth factor, and interleukin 6 in Meigs syndrome. *Am J Obstet Gynecol*. 2001;184:354-355.

8. Maryniak A, Oleszak F, Biskupski P, Wengrofsky P, Lee Y. Cardiac tamponade unmasking recurrent ovarian cancer. *Cureus*. 2021;13:e15464.

KEY WORDS cardiac magnetic resonance, electrocardiogram, pericardial effusion, echocardiography, shortness of breath, tamponade